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Award Number: MIPR 4CSNCM4035

TITLE: DoD-Wide Medical Surveillance for Potential Long-Term Adverse Events Associated with Smallpox Vaccination, Hospitalizations, and Self-Reported Outcomes

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REPORT DATE: January 2005

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	January 2005	Annual (1 Jan 2004 - 31 Dec 2004)

4. TITLE AND SUBTITLE
DoD-Wide Medical Surveillance for Potential Long-Term Adverse Events Associated with Smallpox Vaccination, Hospitalizations, and Self-Reported Outcomes

5. FUNDING NUMBERS
MIPR 4CSNCM4035

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 Words)
This investigation focuses on potential long term negative health consequences of smallpox vaccination in military personnel who were on active duty in December 2002 when DoD implemented a service-wide smallpox vaccination program. It is designed to complement the collaborative monitoring effort for short-term adverse events associated with the administration of vaccines known as the Vaccine Adverse Events Reporting System (VAERS). The current revised protocol involves surveillance of electronic impatient and outpatient medical records, and evaluation of self-reported symptoms and conditions among smallpox-vaccinated and non-vaccinated active and separated service members who have participated in the Millenium Cohort Study. Investigators will examine the relationship between objective (SIDR, SADR, HCSR records of illness) and subjective outcome data as provided in the Millennium Cohort Study survey both before and after smallpox vaccination.

14. SUBJECT TERMS
Smallpoz Vaccine Surveillance Epidemiology Hospitalization

15. NUMBER OF PAGES
7

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

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INTRODUCTION

Although naturally occurring smallpox was eradicated worldwide in 1977, perceived terrorist threats of biological weapons use prompted the FDA to license a reformulated smallpox vaccine, Dryvax®, in 2002. Following licensure, the Department of Defense (DoD) established the Smallpox Vaccination Program on 13 December 2002 as a safeguard against the potential risk of a smallpox attack aimed at US military personnel. As of 16 September 2004, approximately 641,000 service members have received the smallpox vaccine.

In a collaborative effort with the CDC and FDA, the DoD currently monitors short-term adverse events associated with the administration of vaccines through the Vaccine Adverse Events Reporting System (VAERS). However, a surveillance system to monitor the long-term adverse health outcomes associated with vaccinations is lacking. This investigation is designed to assess the long-term safety of the smallpox vaccine.

Objectives:

We propose to complement VAERS surveillance as managed by the DoD, CDC, and FDA, and designed to identify short-term, sentinel events associated with vaccine usage. The current study will assess objective and self-reported adverse health events of a long-term nature, in terms of potential associations with smallpox vaccination.

RESEARCH METHODS

Historical Prospective Study

The cohort will include all US military personnel serving on active duty as of 01 January 2002. Using existing military databases, we will obtain medical inpatient and outpatient discharge diagnoses, as well as demographic, occupational, and deployment information, for smallpox vaccinated and non-vaccinated active-duty service members.

Self-Reported Outcomes

For the self-reported outcomes portion of this study, we originally proposed a postal survey of 5,000 randomly selected service members, half of who would have been vaccinated against smallpox and half of whom would not. By design a proportion of targeted subjects would be on active duty when the questionnaire was mailed and some would have already separated. Regulations thus required approval from both the Defense Manpower Data Center and from the Office of Management and Budget before the survey could be implemented. While waiting for the approval to be granted it was decided that the study's objectives might more efficiently be achieved through use of already collected survey data available from Panel 1, Waves 1 and 2, of the Millennium Cohort Study. Therefore, a revision of the protocol was drafted to reflect these different methods, submitted to the Naval Health Research Center IRB, and approved (See attached – appendix A). The same revision was submitted to the HSSRB at Fort Detrick for review. Approval from the funding source came this week on December 17, 2004. (See attached – appendix B)

Healthcare Utilization Data

Data use agreements between the DoD Center for Deployment Health Research and TriCare M2 are in place and support ongoing extraction of inpatient and outpatient electronic medical records from SIDR, SADR and HCSR tables, as well as from DEERS. An immunization data file covering the period from January 1 1998 through December 31 2003 already exists at the Center and is semi-annually updated by DEERS.

Self-reported Health Status Data

Respondents in first panel of the Millennium Cohort Study number 77,000. Of these more than 35,000 have submitted a first follow-up questionnaire. Exact numbers of smallpox vaccinees have yet to be established but certainly will be sufficient to address the study's hypotheses.

BODY OF REPORT

Methods are described in the protocol.

Results will be reported following data collection and analyses.

KEY RESEARCH ACCOMPLISHMENTS

Study will be implemented in early 2005. Completion of data collection and analyses to follow.

REPORTABLE OUTCOMES

There are no reportable outcomes at this time.

CONCLUSIONS

None as yet.

Appendix A – Naval Health Research Center IRB Approval of modified protocol

APPENDIX D. POSTAPPROVAL DOCUMENTATION

INSTITUTIONAL REVIEW BOARD RECOMMENDATION

CONTINUING REVIEW / PROTOCOL MODIFICATION

Date of Review: 26 October 2004 Protocol Number: NHRC.2004.0010

Title of Research Protocol: DoD-wide Surveillance for Potential Long-Term Adverse Events Associated with Smallpox Vaccination: Hospitalizations and Self-Reported Outcomes

Principal Investigator: LTCOL Timothy S. Wells, USAF, BSC

Work Unit Title and Number: Deployment Health Research Studies, 60002

Approximate Dates of the Research: January 2004 to December 2006

No. of Previous Reviews: 1

The principal investigator submitted this protocol for continuing review. The objective of this protocol is to extract and analyze objective and self-reported adverse health events occurring over extended periods of time subsequent to smallpox vaccination. Data will be obtained from existing medical and personnel history electronic databases maintained by the Department of Defense as well as from responses received to a health-related questionnaire.

The Continuing Review submission requests the following change: instead of conducting a new postal survey as was originally intended, responses received from military personnel participating in the Millennium Cohort survey study will now be used to supplement the electronic data on vaccinations and inpatient and outpatient visits that are maintained by the Department of Defense. Participants in the Millennium Cohort survey voluntarily filled out questionnaires seeking self-report information about their health after being informed that this information would be linked with data on military service, deployments, and health care records.

This study will utilize existing DoD data sources, and no individual military member will be contacted. The study has been classified as minimal risk, contact with each person whose medical records will be analyzed can not be practicably carried out because of the large numbers of record holders involved, and waiver of informed consent will not adversely affect the rights and welfare of those record holders. Based on these criteria, the provisions of 32 CFR Part 219.116 have been met and informed consent has been waived. The principal investigator indicated compliance with all relevant human subject protection regulations in the submission application.

The Chair reviewed this continuing review under the expedited review authority subdelegated by the Naval Health Research Center Commanding Officer and permitted under 32 CFR § 219.110. The Chair recommends approval of the changes and continuation of this study.

The next scheduled review is on or before 25 October 2005.

Christopher G. Blood, J.D., M.A.
Chair, NHRC IRB

Signature & Date

APPENDIX B – Notice of USAMMRMC Approval of Revised Protocol

-----Original Message-----
From: Duchesneau, Caryn L Ms USAMRMC [mailto:caryn.duchesneau@us.army.mil]
Sent: Friday, December 17, 2004 2:27 PM
To: Wells, Tim LTCOL
Cc: Fisher, Pam L Ms USAMRAA; Carpenter, Calvin B LTC USAMRMC; Brosch, Laura R COL USAMRMC; Duchesneau, Caryn L Ms USAMRMC; clark@nhrc.navy.mil; Bennett, Jodi H Ms USAMRMC
Subject: A-12499 Approval Memo (Proposal Log Number PR033348, Award Number MIPR4CSNCM4035)

SUBJECT: HSRRB Approval of Protocol "DoD-Wide Medical Surveillance for Potential Long-Term Adverse Events Associated with Smallpox Vaccination, Hospitalizations and Self-Reported Outcomes," Submitted by Timothy Wells, LtCol, USAF, BSC, DoD Center for Deployment Health Research, San Diego, California, Proposal Log Number PR033348, Award Number MIPR4CSNCM4035, HSRRB Log Number A-12499

1. Revisions to the subject protocol received on 6 December 2004 have been reviewed for compliance with applicable human subjects protection regulations. Documentation of the IRB of Record's approval of this version of the protocol was received on 17 December 2004.

2. In accordance with 32 CFR 219.110 (a, b), this protocol should be approved by expedited review because it involves no more than minimal risk and is one of the categories of research listed in the November 9, 1998 Notice in the Federal Register (63 FR 60364-60367) that may be reviewed by the IRB through an expedited review procedure. Specifically, it involves research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

3. Informed consent procedure should be waived for this protocol in accordance with the stipulations found in 32 CFR 219.116 (d) because the research involves no more than minimal risk to the subjects, the waiver or alteration will not adversely affect the rights and welfare of the subjects, and the research could not practicably be carried out without the waiver or alteration.

4. There are no outstanding human subjects protection issues to be resolved. The study is approved for use with human subjects.

5. Submission of the Volunteer Registry Data Base sheet is not required for this study.

6. In accordance with 32 Code of Federal Regulations 219, a continuing review report must be submitted to the local Institutional Review Board. According to our records, the continuing review report is due to the Naval Health Research Center IRB on or before 25 October 2005. A copy of the continuing review report and the Naval Health Research Center IRB approval of that report, is to be forwarded to the Acting Chair, HSRRB as soon as possible after local approval is obtained.

7. Any protocol modifications (including but not limited to changes in the principal investigator, inclusion/exclusion criteria, number of subjects to be enrolled, study sites, or procedures) must be submitted as a written amendment for HSRRB review and approval before implementing the change.

8. The point of contact for this approval is Mr. Tibor Tuzson at 301-619-6192.

Caryn L. Duchesneau, CIP
Vice Acting Chair, Human Subjects
Research Review Board

Note: The official signed copy of this approval is housed with the protocol file at the Office of Research Protections, 504 Scott Street, Fort Detrick, MD, 21702. Signed copies will be provided upon request.